Is oral lornoxicam effective in the treatment of acute migraine attacks? : a randomized-controlled study

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IS ORAL LORNOXCAM EFFECTIVE IN THE TREATMENT OF ACUTE MIGRAINE ATTACKS? : A RANDOMIZED-CONTROLLED STUDY

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ABSTRACT

Objective: The aim of this study was to assess the efficacy of lornoxicam (LNX) in the treatment of acute migraine attacks. Material and Methods: This prospective, randomized, double-blind, placebo-controlled trial was conducted administering either LNX or placebo to patients who were diagnosed with migraine without aura according to the International Headache Society (the year 2004) criteria between 2010 and 2012. Results: Of 44 patients with 120 migraine attacks, 38 were female and rest were males. Mean age was 37.75 ± 9.28 years. Patients recorded using LNX in 87 migraine attacks and placebo in 33 migraine attacks, respectively. Pain intensity scores of the patients were found similar between LNX and placebo groups, statistically. Conclusion: Although oral LNX was found to have efficacy similar to placebo statistically in the treatment of acute migraine attacks, further studies are needed to evaluate appropriately the efficacy of LNX for treatment of acute migraine attacks.

Key Words: Lornoxicam, migraine, acute attack, treatment efficacy

INTRODUCTION

Migraine is a common cause of headache. Prevalence of migraine is reported to be 11% in the adult population in the studies from western countries. The study, which was conducted by Turkish headache epidemiology study group reported the incidence of migraine to be 16.4% between 15-65 years old. It is seen three times more in women than men, and it often occurs between the ages of 25 to 55 years. Migraine treatments are generally based on two major groups, including non-pharmacological and pharmacological methods. Pharmacological treatment is divided into two groups; prophylactic and acute attack treatment. Acute migraine attacks should be managed rapidly and effectively. Therapy is considered to be successful when there is decrease in the frequency and severity of attacks. Acute attack treatment should be tailored to the patients systemic disease and symptoms as well as the severity, duration and frequency of the attacks. In mild and moderate attacks, non-specific therapy non-steroidal anti-inflammatory drugs (NSAIDs) alone or in combination with either caffeine or codeine may be used. Moderate and severe attacks which cannot be prevented with nonspecific migraine drugs are managed with specific drugs such as triptans or ergot derivatives.

Although the central effects of NSAIDs are not exactly known, three mechanisms are mainly emphasized. These are the inhibition of central nervous system prostaglandin synthesis by NSAIDs, the increasing of CNS catecholamine and serotonin cycle, and the inhibition of serotonin release during pain stimulus. Lornoxicam (LNX) (6-chloro-4-hydroxy 2-methyl N-pyridyl 2H-thienol (2, 3 e) 1, 2-thazine 2-karbaksamid 1, 1-dioxide), is a NSAID drug in non-selective, oxicam group according to former classification. LNX has potent anti-inflammatory and analgesic effects similar to other oxicams but unlike them it has a shorter half life (3-5 hours). Both oral and parenteral preparations are used. LNX has a better tolerability profile compared with other oxicam drugs because of shorter half life. Clinical trials suggest LNX as an effective drug in the treatment of post-operative and joint pains. The aim of this study was to assess the efficacy of LNX in treatment of headaches due to acute migraine attacks.

MATERIAL AND METHODS

This is a prospective, randomized, double-blind, placebo-controlled study conducted by department of clinical of algology, school of medicine Istanbul University and department of neurology, Ministry of
Health Dr. Sadi Konuk Research and Training Hospital between January 2010 and December 2012. Inclusion criteria was:

- age between 18 and 65 years,
- being diagnosed with migraine without aura according to the International Headache Society criteria (the year 2004),
- having experience of first headache attack before 50 years of age,
- having moderate to severe migraine attacks with frequency less than 4 times per month.

This study was approved by ethics committee that was established in the School of Medicine, Istanbul University. Randomization table has been used for randomization of the patients. Diagnosis of migraine of the included patients was done by a neurology physician. Patients’ migraine attacks were recorded to assess the effectiveness of LOLA. After being informed about the study, all volunteers were asked to sign the "informed consent form". Patients’ physical examinations, pulse rates and blood pressure of patients as well as medical history regarding usage of drug or non-drug medications and simultaneous systemic diseases were recorded during all visits. Patients who were pregnant, nursing and planning to be pregnant during the study, not informed about treatment sufficiently, used different treatment for migraine attacks, and who quitted the follow-up were excluded from the study. Patients received two different blisters containing either placebo or the study drug (8 mg LNX) for two migraine attacks during first and second visits. The 3rd visit was arranged at the end of the fourth week or within five days after second attack and the 4th visit was arranged at the end of the eighth week or within five days after third attack. They were allowed to use maximum two tablets in a day. If headache persisted despite the use of the two tablets given for the study, they were permitted to use eletriptan 40 mg as a subsidiary medicine at least an hour after the second tablet. Patients were inquired which blister they had taken if they had headache attack and whether they had taken one more tablet from blisters when headache persisted for three hours. Migraine attacks of patients which were not recorded during follow up were not evaluated. Pain intensity score was rated from 0 to 3 points (0= none, 1= mild, 2= moderate, 3= severe) in the survey. Headache severity was evaluated with a questionnaire performed before taking the drug at 0 min and at 15th, 30th, 60th, 90th minutes and at 2nd, 3th, 6th, 12th, 24th hours after the administration of drug. Pain relief was assessed with a rating system of 5 points (0= none, improvement; 1= a little, 2= some, 3= a lot, 4= complete, and worsening; -1= a little, -2= some, -3= a lot, -4= complete) after the administration of drug at 15 th, 30 th, 60 th, 90 th minutes and at 2 nd, 3 th, 6 th, 12 th, 24 th hours. Evaluation of patient satisfaction was assessed at the end of the 24-h period (1= satisfied, 2= unsatisfied).

A Statistical Analysis
Age was expressed as mean ± standard deviation. Changes in headache severity were assessed by Mann-Whitney U test in the pre-treatment period and after the treatment at 15 th, 30 th, 60 th, 90 th minutes and 2nd, 3th, 6th, 12th, 24th hours. Characteristics of patient and placebo groups and satisfaction with the treatment between placebo and treatment group was assessed by Chi-square test. Statistical significance was determined at p < 0.05.

Table 1: Demographic characteristics of the study participants.

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=14)</th>
<th>LNX (n=30)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female/Male</td>
<td>11/3</td>
<td>27/3</td>
<td>0.364</td>
</tr>
<tr>
<td>Age (years; mean ± SD)</td>
<td>37.9 ± 10.1</td>
<td>37.5 ± 8.4</td>
<td>0.902</td>
</tr>
<tr>
<td>Illiterate</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Elementary School</td>
<td>10</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>High School</td>
<td>-</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>University</td>
<td>2</td>
<td>9</td>
<td></td>
</tr>
</tbody>
</table>

RESULTS
During the study period, 6 of 50 patients were excluded from the study due to excluding criteria. Of 44 patients whose 120 migraine attacks were evaluated, 38 were females. Mean age 37.75 ± 9.28 years. Characteristics of patients have been shown in Table 1. There was no comorbidity in both patient and placebo groups. During the study period, LNX was used in the 87 attacks, placebo was used in the 33 attacks. The number of headache attacks in which placebo and LNX were used is given in Table 2.

Evaluation of patients’ pain intensity scores
The severity of the headache was assessed individually after administration of the first dose at the beginning, 15th, 30th, 60th, 90th minutes and the 2nd, 3th, 6th, 12th, 24th hours in both groups. There was not found difference between pain intensity scores which were surveyed after LNX and placebo treatments, statistically (Table 3).
Evaluation of patients’ pain relief scores
The pain relief was assessed individually after administration of the first dose at 15th, 30th, 60th, 90th minutes and the 2nd, 3th, 6th, 12th, 24th hours in both groups. There was not found any difference between pain intensity scores which were surveyed after LNX and placebo treatments, statistically (Table 4).

Evaluation of patients’ satisfaction scores
Patients’ satisfaction scores were insignificant between LNX and placebo treatments, statistically (Table 5).

Evaluation of drug associated side-effects
No adverse reactions were with both placebo treatment and LNX treatment.

Table 2: Distribution of the number of migraine attacks in which LNX and placebo treatments were given

<table>
<thead>
<tr>
<th>The number of migraine attacks</th>
<th>Placebo</th>
<th>LNX</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13</td>
<td>29</td>
<td>0.360</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>20</td>
<td>0.360</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>26</td>
<td>0.360</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>12</td>
<td>0.360</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>87</td>
<td>0.360</td>
</tr>
</tbody>
</table>

DISCUSSION
LNX has been evaluated for the first time in terms of its efficacy and side-effects, due to the fact that there has been no study about it in the treatment of acute migraine attacks. In context with that although NSAIDs were presented to be effective in the treatment of acute migraine attacks, serum level concentration of LNX should be measured after oral use to evaluate the efficacy appropriately. Since oral usage of LNX cannot reach therapeutic blood concentration rapidly and sufficiently despite its short and rapid time of action, because of first-pass elimination. Also a parenteral form of LNX may be evaluated or compared with oral form to reveal its effectiveness and whether the administration route is important or not. Despite studies showing the effectiveness of oral administration of LNX are associated with pains other than migraine it is important to ensure early, rapid and effective plasma concentration in pains related to migraine. NSAIDs in the oxicam groups were reported to be effective for acute migraine attacks. In a study conducted by CY et al the effectiveness of celecoxib and naproxen sodium in the treatment of acute migraine was investigated. Both drugs were found to be equally effective in the treatment of acute migraine, but epigastric pain was found significantly higher in the naproxen sodium group.

Ravishankar and colleagues evaluated the efficacy of sublingual piroxicam in patients suffering from migraine without aura. In their study, either piroxicam 40 mg or placebo was administered randomly and double-blind to 60 patients who were suffering from two to 16 migraine attacks per month without aura at age 18-50 years. The severity of the pain was evaluated using the visual analogue scale (VAS). This study described the decrease in pain intensity at 15 min and even 24 hours after sublingual piroxicam administration. This decrease was statistically significant compared to placebo. Ravishankar and his colleagues administered placebo and the drug in different patient groups, whereas drug and placebo were administered to the same group of patients in our study. The small population size and administration of both the drug and placebo into a group of patients are likely to be related to this insignificance. Although mean age and the number of migraine attacks in our study were similar to Ravinshankar’s study, sublingual form is likely to cause to different results compared to oral form as well. Since the administration of piroxicam sublingually reaches an effective blood plasma concentration without being exposed to the first-pass elimination in the liver. The side-effect did not develop in our study. In a study comparing of LNX with intravenous morphine in the treatment of post operative pain, LNX was found to provide similar analgesic effect with a lower incidence of adverse events. Adverse effects, such as nausea, vomiting, gastritis, heartburn, and diarrhea were reported to develop less with a sublingual form of LNX than naproxen sodium in the study of Aabakken et al.

In a study performed on healthy volunteers, it has been verified that less gastro-duodenal injury developed with LNX (16 mg / day) compared to naproxen sodium (1000 mg / day). The limitations of our study are small population size, administration of both drug and placebo in some cases, usage of only oral form of LNX. Intravenous form of LNX should be evaluated in terms of efficacy and side-effects compared with oral forms of LNX with a randomized-controlled study for treatment of acute migraine attacks. As a result, although oral LNX was found to have efficacy similar to placebo statistically in the treatment of acute migraine attacks, further studies are needed, including two different groups, two forms and different dosages of LNX to evaluate appropriately the efficacy of LNX for treatment of acute migraine attacks.
ACKNOWLEDGEMENTS

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Table 3: Evaluation of patients’ pain intensity scores after LNX and placebo treatments

<table>
<thead>
<tr>
<th>Post-treatment</th>
<th>Pain intensity score</th>
<th>Beginning (n,%): Placebo</th>
<th>15-min (n,%): Placebo</th>
<th>30-min (n,%): Placebo</th>
<th>60-min (n,%): Placebo</th>
<th>90-min (n,%): Placebo</th>
<th>2-h (n,%): Placebo</th>
<th>3-h (n,%): Placebo</th>
<th>6-h (n,%): Placebo</th>
<th>12-h (n,%): Placebo</th>
<th>24-h (n,%): Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Group 1</td>
<td>4 (12.1)</td>
<td>5 (15.6)</td>
<td>7 (21.9)</td>
<td>9 (28.1)</td>
<td>7 (25)</td>
<td>5 (16.7)</td>
<td>8 (33.3)</td>
<td>3 (37.5)</td>
<td>2 (33.3)</td>
<td>3 (50)</td>
<td>3 (50)</td>
</tr>
<tr>
<td>Group 2</td>
<td>16 (48.5)</td>
<td>17 (53.1)</td>
<td>16 (50)</td>
<td>13 (40.6)</td>
<td>11 (39.3)</td>
<td>12 (40)</td>
<td>8 (33.3)</td>
<td>1 (12.5)</td>
<td>1 (16.7)</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Group 3</td>
<td>13 (39.4)</td>
<td>10 (31.3)</td>
<td>8 (25)</td>
<td>8 (25)</td>
<td>7 (25)</td>
<td>11 (36.6)</td>
<td>6 (25.1)</td>
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<td>17 (20.5)</td>
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<td>21 (31.8)</td>
<td>20 (26.7)</td>
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<td>6 (18.2)</td>
<td>8 (28.6)</td>
<td>6 (24)</td>
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<td>Group 2</td>
<td>44 (50.6)</td>
<td>38 (45.8)</td>
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<td>23 (34.9)</td>
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<td>Group 3</td>
<td>30 (34.5)</td>
<td>33 (39.7)</td>
<td>32 (36.8)</td>
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<td>18 (27.3)</td>
<td>22 (29.3)</td>
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<td>4 (12.1)</td>
<td>3 (10.7)</td>
<td>4 (16)</td>
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Table 4: The pain relief scores of the cases after LNX and placebo treatments

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<tr>
<th>Post-treatment</th>
<th>Pain relief score</th>
<th>15 min (n, %)</th>
<th>30 min (n, %)</th>
<th>60 min (n, %)</th>
<th>90 min (n, %)</th>
<th>2 h (n, %)</th>
<th>3 h (n, %)</th>
<th>6 h (n, %)</th>
<th>12 h (n, %)</th>
<th>24 h (n, %)</th>
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</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>4</td>
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<td>-</td>
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<td>-</td>
<td>-</td>
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</tr>
<tr>
<td>Treatment</td>
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<td>1 (3.1)</td>
<td>-</td>
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<tr>
<td>2</td>
<td>1 (3.1)</td>
<td>2 (6.3)</td>
<td>4 (12.5)</td>
<td>5 (17.9)</td>
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<td>6 (25)</td>
<td>1 (12.5)</td>
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<td>9 (30)</td>
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<td>0</td>
<td>25 (75.1)</td>
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<td>-2</td>
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<td>1 (3.3)</td>
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<tr>
<td>Treatment</td>
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<td>1 (1.2)</td>
<td>4 (4.8)</td>
<td>6 (7.6)</td>
<td>5 (7.6)</td>
<td>9 (12)</td>
<td>11 (18.6)</td>
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<td>11 (39.3)</td>
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<td>1</td>
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<td>36 (45.6)</td>
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<td>33 (44)</td>
<td>20 (33.9)</td>
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<td>0.135</td>
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<td>0.961</td>
<td>0.522</td>
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Table 5: Patients’ satisfaction scores

<table>
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<tr>
<th>Satisfied/Unsatisfied</th>
<th>Placebo</th>
<th>LNX</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>%</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Satisfied</td>
<td>18</td>
<td>54.5</td>
<td>48</td>
</tr>
<tr>
<td>Unsatisfied</td>
<td>15</td>
<td>45.5</td>
<td>39</td>
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<tr>
<td>Total</td>
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<td>p</td>
<td>0.690</td>
<td></td>
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</table>
improvement as well as decreasing levels of ammonia. 21
in 2011 supported the use of LOLA for neuro-psychiatric
cencephalopathy, causes both clinical and biochemical
randomized clinical trials including 646 patients that,
studies. Bai et al concluded after meta-analysis of 8
infusion of LOLA. These results were comparable to other
In our study, it was observed that the LOLA has beneficial
is a major cause of hepatic encephalopathy, that's why
complication in CLD. High levels of ammonia in the body
prevalent compared to developed countries. 17 In fact both
infected people and cirrhotics are common in our community. 18, 19
value < 0.05. (Table: III)
standard treatment regimen.
encephalopathy especially when not responsive to
may be used in the patients with hepatic
amino acids.
standard treatment of hepatic encephalopathy like
lactitol, rifixamine, Zinc supplements and branch chain
analysis, we can recommend use of LOLA as addition to
other national and international studies and meta
concluded that LOLA was safe and associated with rapid

RESULT

placebo were compared by paired t-test. A p-value of <
treatment with Ornithine - Aspartate infusion and on
plasma. The testing was performed at a reliable
dehydrogenase in a rapid and interference –
infusions were given at the
spleen and portal vein. Trial-Treatment group received a
daily intravenous infusion of 20 g (4 ampoules)
imbalance, prolonged prothrombin time were treated


tilt-Hansen P, Welch KMA (eds.) The
Tfelt-Hansen P, Rolan P Nonsteroidal
anti-inflammatory drugs in the acute treatment of
migraines. In, Olesen J, Goadsby PJ, Ramadan
Tfelt-Hansen P, Welch KMA (eds.) The
Chandrasekharan NV, Dai H, Roos KL, Evanson NK,
Tomsik J, Elton TS, Simmons DL. COX-3, a
cyclooxygenase-1 variant inhibited by
acetaminophen and other analgesic/antipyretic
drugs: cloning, structure, and expression. Proc Natl
8. Bolukbasi N, Ersanli S, Basegmez C, Ozdemir T, 
Ozalcin S. Efficacy of quick-release lornoxicam
versus placebo for acute pain management after
dental implant surgery: a randomised
placebo-controlled triple-blind trial. Eur J Oral
9. Aabakken L, Osnes M, Frenzel W. Gastrointestinal
tolerability of lornoxicam compared to that of
naproxen in healthy male volunteers. Aliment
10. Rosenow DE, Albrechtsen M, Stolke D. A
comparsion of patient-controlled analgesia with
lornoxicam versus morphine in patients undergoing
1045-1050.
11. Loo CY, Tan HJ, Teh HS, Raymond AA. Randomised,
open label, controlled trial of celecoxib in the
treatment of acute migraine. Singapore Med J.
2007;48(9):834-839.
12. Ravishankar K, Tayade H, Mandlik R. Sublingual
piroxicam in migraine without aura. J Assoc
Physicians India. 2011;59:494-497.

REFERENCES

1. Scher AI, Stewart WF, Lipton RB. Migraine and
headache: a meta-analytic approach. In: Crombie
IK (ed) Epidemiology of pain, Seattle: WA, IASP
2. Siva A. Baş ağrısı epidemiyolojisi. Baş, boyun ve
3. Lipton RB, Bigal ME. Migraine: epidemiology,
impact, and risk factors for progression.
4. Lipton RB, Bigal ME, Steiner TJ, Silberstein SD,
Olesen J. Classification of primary headaches.
5. Mathew NT, Tfelt-Hansen P General and
pharmacological approach to migraine
management. In, Olesen J, Goadsby PJ, Ramadan
NM, Tfelt-Hansen P, Welch KMA (eds.) The
anti-inflammatory drugs in the acute treatment of
migraines. In, Olesen J, Goadsby PJ, Ramadan NM,
Tfelt-Hansen P, Welch KMA (eds.) The
7. Chandrasekharan NV, Dai H, Roos KL, Evanson NK,